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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,571	01/21/2004	Swapan K. Ghosh	19026-14	3465

30565 7590 06/06/2005

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EXAMINER

TONGUE, LAKIA J

ART UNIT PAPER NUMBER

1645

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/761,571

Applicant(s)

GHOSH, SWAPAN K.

Examiner

Lakia J. Tongue

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 27-56 is/are pending in the application.
- 4a) Of the above claim(s) 2, 3, 50-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4-16, 27-49 and 54-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's response filed on February 14, 2005 is acknowledged. Claims 1-16, 27-49 and newly added claims 54-56 are under examination as they relate to the elected species phytol derivative. Claims 2, 3 and 50-53 are withdrawn as they are drawn to non-elected subject matter. Claims 17-26 have been canceled and withdrawn from consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections Withdrawn

2. In view of applicant's response the objections to the specification, page 2, paragraph 2 and the claim objection, page 3, paragraph 3 is withdrawn.

Objection Maintained

3. The objection to the Information Disclosure Statement for the reasons set forth on page 2, paragraph 1 is maintained.

Rejections Withdrawn

4. In view of applicant's response the rejections over Franchini et al page 9, Lenk et al page 10 and Danilov et al page 10 all under 35 U.S.C. 102 have been withdrawn.

Rejection Maintained

5. The rejection of claims 1, 4-16, 27-49 and newly added 54-56 under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement is maintained.

The rejection was on the ground that the specification lacks guidance and teaching to show that, for example, the composition comprising a phytol derivative as adjuvant and a vaccine antigen, e.g. HIV antigen, was generated or extracted and used to prevent infection (as would be expected from a "vaccine" antigen preparation).

The obstacles to vaccine development and therapeutic approaches with regard to retroviruses associated with AIDS in humans are well documented in the literature. These obstacles include: 1) the extensive genomic diversity associated with the HIV retrovirus, particularly with respect to the gene encoding the envelop protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to "hide" in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the retrovirus, due to the blood-brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or any immunization treatment or any therapeutic regimen on its face. By definition vaccines must not only induce an immune response, but must be immunogenic to the extent that upon subsequent challenge with the live virus, development of the disease is prevented, or better yet infectivity does not occur. Fox (1994, BioTechnology 12:128) has reported on investigations reported by attendees at the First National Conference on Human Retroviruses and Related Infections and the frustrations encountered by several investigators. Those attending the conference have agreed that despite positive results coming from several laboratories, "AIDS researchers inevitably come back to the conference's central theme. No therapy had emerged as a sure winner in the campaign against HIV, not a preventive vaccine nor therapeutic vaccine nor any of the immune-system-boosting treatments." Thus it is clear that one would not accept claims to a vaccine or therapeutic against HIV on its face, absent evidence to the contrary.

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Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). In the instant specification 1) insufficient direction or guidance is presented in the specification with respect to selecting other immunomodulators having the claimed functional feature of effectiveness in treating or preventing HIV infection, 2) there are no working examples which suggest the desired results of a vaccine antigen effective in treating or preventing HIV infection, 3) the nature of the invention involved the complex and incompletely understood area of immune correlates to HIV infection, 4) the state of the art shows that prior vaccines and treatment therapies have been largely ineffective for the intended purpose, 5) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level), and 6) the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by prior failures.

The claims also do not exclude a composition comprising a phytol derivative and a Plasmodium falciparum vaccine antigen. The obstacles to development of vaccines against malaria have also been well documented. Hodder, et al, 1996, investigated the disulfide bond structure of Plasmodium AMA-1 antigen and stated (page 29452) "We are currently producing the putative domains in an *E. coli* expression system...in an effort to establish which regions of the molecule are most relevant for the generation of protective immune responses."

It is apparent, from this report, that protective immune response to Plasmodium falciparum antigen are still in the investigation stage and that one skilled in the art would not readily accept claims to vaccines protecting against human malaria, absent evidence to the contrary, as being enabling.

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). In the instant specification there are no working examples which would suggest a vaccine against human malaria, the nature of the invention involves complex and incompletely understood areas of immunity to malaria, the state of the art shows that vaccines against human malaria are still in the developmental stage, the relative skill in the art is recognized as quite high (post-doctoral level) and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the lack of correlation between the generation of antibodies against malaria antigens and protection. Therefore, in view of all of the above, it is determined that it would require undue experimentation to make and use the claimed compositions comprising a vaccine antigen to protect against all type of disease including HIV and malaria caused by Plasmodium species.

Applicant urges that claim 1 has been amended to recite that the composition comprises a vaccine preparation effective for the treatment of a mammal.

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It is the examiner's position that the claims are still drawn to a vaccine preparation. This recitation includes any and all vaccines, including HIV antigens. There is no known effective vaccine or treatment for HIV. The amendment does not overcome the claimed vaccine preparation. Applicant may want to consider revising the claim language. Suggested language is as follows:

A composition comprising a preparation effective for treatment of a mammal in unit dosage form including:

An effective amount of an antigen;

An adjuvant component comprising phytol, isophytol, or a phytol derivative, said antigen homogenously dispersed in the adjuvant component; and optionally a carrier.

6. It should be noted that the 102(b) rejection over Stewart, Jr. et al (U.S. 6,406,885) should read Stewart in light of Takayuki Suga et al. The examiner regrets this oversight.

The rejection of claims 1, 6-11 and 27-49 and newly submitted claim 56 under 35 U.S.C. 102(b) is maintained for the reasons set forth in the previous Office Action page 8, paragraph 5.

The rejection was on the ground that Stewart, Jr. et al disclose engineered plants (soybean) expressing intimin antigen or the intimin fusion protein from *e.coli*. After the transformation of the soybean it is then fed to animals and/or humans to elicit the production of antibodies. Stewart, Jr. et al disclose that the antigens may derive from but are not limited to bacteria, rickettsiae, fungi, viruses, parasites, drugs or chemicals. They may include small molecules such as peptides, oligosaccharides and toxins (column 23, lines 17-20). Additionally, in example XI Stewart Jr, et al discloses a gene gun-mediated transformation of various plants. Stewart Jr. et al disclose a method of transforming plants to express intimin or intimin fusion proteins. The plasmid is coated

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onto microparticles, one gram of soybean embryos initiated from immature cotyledons and then are fed to animals, such as pigs (column 43, lines 15-37).

The composition inherently contains the phytol derivative because Suga et al. shows soybean comprising polyprenols in the structure found on page 3391, which is the same as the claimed structure in claim 6 of the instant application. Characteristics such as T-independent antigens, polypeptides and proteins are inherent in the composition of Stewart et al.

Applicant urges that neither of the references either consider singly or together disclose or suggest a composition as instantly claimed with a vaccine in a unit dosage form.

It is that examiner's position that Stewart et al composition with phytol showed that soybean contained phytol derivatives. The intimin would inherently be effective for the treatment of a mammal. The recitation of "antigen homogenously dispersed in the adjuvant component" is being viewed as a process limitation. The preparation of a composition does not make the composition different or render it novel. There is nothing on the record to show (via a side-by-side comparison) that the composition of the prior art would not be effective for the treatment of a mammal.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 54 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear how an ion can be attached to a carbon, as this is an unnatural link.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakia J. Tongue whose telephone number is 571-272-2921. The examiner can normally be reached on Monday-Friday 7-3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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